

## **REMARKS**

### **I. Introduction:**

Claims 1, 17, 19, 31, 42, 47, and 52 are amended and claim 2 is cancelled herein. Claims 38-41 have been previously withdrawn from consideration by the Examiner as being directed to a non-elected distinct invention. With entry of this amendment, claims 1, 3-37, and 42-53 will be pending.

### **II. Claim Rejections Under 35 U.S.C. §102(b):**

Claims 1, 2, 10, 17-19, 21-25, 29, 31, 33-35, 37, 42-47, 49, and 51-53 stand rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 5,324,483 (Cody et al.).

Claim 1 generally requires a base having a plurality of reaction wells formed therein, a cover configured for sealing engagement with the base to form a housing and define a common pressure chamber in communication with the reaction wells, and an inlet port in communication with the pressure chamber for supplying pressurized fluid to the chamber to pressurize the reaction wells. Each of the reaction wells has a closed lower end and an open upper end for receiving components for a reaction. Claim 1 has been amended to specify that the material and structure of the pressure chamber is such that the chamber is operable to sustain an operating pressure above 40 psig.

Applicants respectfully submit that the apparatus as set forth in claim 1 is not anticipated by Cody et al., which disclose an apparatus for solid phase synthesis. The importance of the explicit description in Cody et al. of the use of the apparatus for solid phase synthesis is that pressurization substantially above atmospheric pressure is not required. Furthermore, as is clear from the drawings and description of the apparatus, the apparatus is not designed to sustain pressure

substantially above atmospheric pressure, and especially not greater than 40 psig (which is equal to 54.7 psia).

The apparatus includes a reservoir block 15 having a plurality of wells 16, a plurality of reaction tubes 11 with filters 14 on their lower ends, a holder block 18 having a plurality of apertures 19, and a manifold 20 which may include ports 23 to allow introduction or maintenance of a controlled environment (see Figs. 1 and 3). The Cody et al. patent is directed to solid phase synthesis which focuses on chemical reactions of substrates attached to solid supports (e.g., polystyrene, polyethylene glycol, cellulose, controlled-pore glass), including methods for attachment and detachment from the supports. [See, for example, col. 2, lines 56-68, col. 3, lines 4-6 ("The approach described herein greatly increases the flexibility and diversity of structures that can be produced by a parallel, solid phase synthesis technology."), col. 3, lines 10-15 ("The key feature [] provides a unique means to segregate and manipulate the growing compounds on a solid support.".)] The background of Cody et al. specifies conditions for the synthesis of general organic compounds, which do not include pressurization substantially above atmospheric pressure. [See, col. 1, line 67 - col. 2, line 2.] This is because solid phase synthesis applications generally do not use a pressurized reacting gas. Moreover, Cody et al. are concerned with the synthesis of small organic molecules and not gas phase polymerization. [See, col. 3, lines 1-3].

As noted by the Examiner, the reaction wells of the Cody et al. apparatus are constructed of a material which is capable of withstanding reactive components and manipulations. The Cody et al. patent specifies that the manifold provides an air-tight chamber which facilitates manipulation common to organic synthesis (col. 9, lines 25-36 ("...The ports (23) allow control over atmosphere within the manifold (20) and provide a means to sparge the reaction tubes (11)."). Gasket 24 is placed between the holder block 18 and manifold 20

to create a sealing effect between the manifold and the holder block to allow manipulations and inert atmosphere (col. 9, lines 46-50). The apparatus of Cody et al. is thus pressurized in the context of manipulation (i.e., forcing liquid contents of reaction wells through filter plate) and not reaction. Manipulation requires only nominal pressure or an inert atmosphere. Cody et al. do not disclose an apparatus configured for pressurization substantially above atmospheric pressure since this is not required for solid phase synthesis.

As further evidence that the apparatus of Cody et al. is not designed to withstand pressure substantially above atmospheric pressure, a preferred embodiment utilizes a piercable septum (gasket) 34 to seal the chamber (Figs. 1 and 6). The gasket 34 may be made from a rubber that is puncturable with a needle-like object and reseals following the puncture (col. 10, lines 7-12). Once the septum is pierced, the chamber will not be able to sustain significant pressures (e.g., above about 1 or 2 psig).

Thus, the apparatus of Cody et al. is configured to sustain only an inert atmosphere or nominal pressures for use in physical manipulation for solid phase synthesis, as is well understood by those skilled in the art. In contrast, applicants' apparatus is designed to sustain an operating pressure above 40 psig and can be used, for example, for gas phase polymerization. The material and structure of the pressure chamber of Cody et al.'s apparatus does not provide a chamber that is operable to sustain an operating pressure above 40 psig. The thickness of the manifold, sealing arrangement between manifold and holder block, and fasteners, which all form the structure of the pressure chamber, are not sufficient to sustain a pressure substantially above atmospheric pressure.

Furthermore, the base of Cody et al. does not include reaction wells formed in an upper surface of the base and extending partially therethrough, with the reaction wells having a closed lower end defined by the base, as required by

claim 1. The closed lower ends of the reaction wells formed by the base in applicants' apparatus provide for a simple, cost effective design which allows for pressurization of the reaction wells with a pressurized gas at a pressure substantially above atmospheric pressure. Since sealing is required only for the common pressure chamber, the apparatus provides increased reliability and simplified maintenance. In contrast, the reservoir block 15 of Cody et al. consists of a reservoir rack 41 which is adapted to hold removable reaction wells 16 (Fig. 5). Without the reaction wells 16 inserted into the base, there is no reaction well formed for holding reaction components.

Accordingly, claim 1 is submitted as patentable over Cody et al. and the other prior art of record.

Claims 2-16 and 27-30 depending either directly or indirectly from claim 1, are submitted as patentable for the reasons discussed above with respect to claim 1.

Claim 31 is directed to an apparatus for use in parallel synthesis of screening materials and generally includes a base member having a cavity formed therein, the cavity having dimensions generally corresponding to a microtiter plate having reaction wells for receiving components of the synthesis or screening, a cover movable between an open and closed position in which the base member and cover form a pressure chamber, an inlet port in communication with the pressure chamber for supplying fluid pressurized substantially above atmospheric pressure to the pressure chamber, and a quick-operating fastening device operable to position the cover in its closed position and hold the cover in sealing engagement with the pressure chamber.

The apparatus set forth in claim 31 is not anticipated by Cody et al., which do not show a base member having a cavity with dimensions generally corresponding to a microtiter plate. The chamber of Cody et al. is formed by

manifold 20 and holder block 18 configured for receiving reaction tubes 11 (Fig. 4). Furthermore, as previously discussed, the apparatus of Cody et al. does not provide a pressure chamber for receiving fluid pressurized substantially above atmospheric pressure.

Accordingly, claim 31 is submitted as patentable over Cody et al. and the other prior art of record.

Claims 32-37, depending either directly or indirectly from claim 31, are submitted as patentable for the same reasons as claim 31.

Claim 17 has been amended to include the limitations of claim 1 and claims 17 and 42 have been amended to specify that the flow restriction device includes a flow passageway formed therein to provide primary flow passages between the reaction wells and the pressure chamber while reducing cross-talk between the reaction wells.

The Examiner identifies gasket 26 of the Cody et al. apparatus as a flow restriction device. Gasket 26 is interposed between the reservoir block 15 and the holder block 18 (Figs. 2, 3, and 5). The gasket 26 does not provide a primary flow passage between the reaction wells and a sealed chamber (i.e., chamber formed by manifold 20). Instead, the reaction tube forms the primary flow passageway. As shown in Fig. 5 and described at col. 9, lines 46-47, gaskets 24 and 26 are used to seal the reaction wells from the chamber. Gasket 26 also seals open ends of the reaction wells 16 from one another. The Examiner states that a slight gap between the gasket 26 and reaction tube 11 allows gas to travel from the pressure chamber into the reaction wells. However, since the gas is generally free to flow between the reaction well and pressure chamber through the reaction tube, there will be little if any fluid communication past the seal.

As noted by Cody et al., the reaction wells should be located throughout the reservoir block such that each reaction well is not in direct contact with any

neighboring reaction wells (col. 8, lines 45-48). Cross-talk which takes place between the reaction wells occurs through the open ends of the reaction tubes, and this cross-talk is not reduced by gasket 26.

Accordingly, claims 17 and 42, as amended, are submitted as patentable over the Cody et al. and the other prior art of record.

Claims 18 and 20-26, depending either directly or indirectly from claim 17, and claims 43-46 and 48-51, depending either directly or indirectly from claim 42, are submitted as patentable for the reasons discussed above with respect to claims 17 and 42.

Claims 19 and 47 have been amended to specify that the flow restriction device includes a plurality of flow passageways aligned with the reaction wells and that each of the flow passageways have a diameter substantially smaller than a diameter of the aligned reaction well. As amended, claims 19 and 47 are submitted as patentable over Cody et al. and the other prior art of record.

Claim 52 is directed to an apparatus for use in parallel reaction of materials and generally requires a base having a plurality of reaction wells formed therein, a cover configured for sealing engagement with the base to form a housing and define a common pressure chamber in communication with the reaction wells, and an inlet port in communication with the pressure chamber for supplying pressurized fluid to the chamber to pressurize the reaction wells. Each of the reaction wells has a permanently closed lower end and an open upper end for receiving components for a reaction. The claim has been amended to specify that the material and structure of the pressure chamber is such that the chamber is operable to sustain a pressure above 40 psig.

Cody et al. do not disclose reaction wells formed in a base and having a permanently closed lower end. The reservoir block 15 of Cody et al. consists of a reservoir rack 41 which is adapted to hold removable reaction wells 16 (Fig. 5).

Without the reaction wells 16 inserted into the base, there is no reaction well formed for holding reaction components.

Furthermore, as previously discussed with respect to claim 1, the apparatus of Cody et al. is not designed to operate at pressures substantially above atmospheric pressure and would not sustain pressures above 40 psig.

Accordingly, claim 52 is submitted as nonobvious and patentable over Cody et al. and the other prior art of record.

Claim 53, depending directly from claim 52, is submitted as patentable for the same reasons as claim 52.

### III. Claim Rejections Under 35 U.S.C. §103(a):

Claims 3-4, 52, and 53 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Cody et al. in view of U.S. Patent No. 5,428,118 (Painter et al.), "Investigation of Coolant Mixing in Pressurized Water Reactors at the Rossendorf Mixing Test Facility ROCOM" (Grunwald et al.), and "Runaway in Stirred Tanks" (Heiszwolf).

Claims 3-4, 52, and 53 all require, among other things, a pressure chamber, wherein the material and structure of the pressure chamber is such that the chamber is operable to sustain a pressure above 40 psig.

Painter et al. disclose a gas phase fluidized bed polyolefin polymerization process using gas or gas-solid tangential flow. Tangential flow of gas is provided in an expanded section of the gas phase reactor to reduce fine entrainment into the gas cycle system and reduce solid particle build-up on interior surfaces of the expanded section of the reactor. A gas phase fluidized bed reactor 1 is used for the process (Fig. 1). A first portion of fluidizing gas is supplied through inlet 13 and a second portion of the gas is supplied to the expanded section of the reactor

via lines connecting to nozzle 6. A compressor 11 and heat exchanger 12 are included to provide gas at different phases to the reactor. The apparatus does not include individual reaction wells for parallel synthesis and is not concerned with sealing individual reaction wells.

The disclosure of Cody et al. is generally limited to solid phase synthesis, whereas Painter et al. deal with gas phase polymerization. The apparatus of Cody et al. is designed to operate at low pressures (e.g., nominal pressure for physical manipulations or inert atmosphere) and would require significant modification for operation substantially above atmospheric pressure, not just with regard to the manifold material but also as to the sealing arrangement and simple spring clips used to hold the assembly together. Since the Painter et al. apparatus does not include a housing containing a plurality of individual reaction wells exposed to a common pressure chamber, it does not address any of the structure concerns that one would have to overcome in making the apparatus of Cody et al. operable to sustain an operating pressure above 40 psig. As previously discussed, not only would the material of the housing of Cody et al. have to be modified, but the structure of the chamber would require significant modification for high pressure operation.

Heiszwolf discusses stability criteria for batch and continuous reactors. The reactor is enclosed by a Plexiglas box to prevent injury to lab personnel in the case of a reactor explosion. The Plexiglas box is not used to create a pressure chamber suitable for sustaining pressure during a reaction. The box is merely provided as a safety precaution in case the actual reactor is over pressurized and explodes. It is used to protect workers from the initial high pressure impact. There is no disclosure of sealing or fastening means which would allow the box to sustain high pressure for any significant period of time, such as required for parallel synthesis and screening of materials.



The Grunwald et al. reference is directed to testing of coolant mixing in nuclear reactors (specifically, pressurized water reactors). First, there is no teaching or suggestion in the cited patents to combine the Grunwald et al. reference, which is directed to nuclear reactors, with Cody et al., which is directed to multiple simultaneous synthesis of compounds. Second, the reference in the Grunwald et al. article to Plexiglas is with regard to a 1:5 scaled test vessel which is operated at ambient pressure with cold water.

Furthermore, the references cited do not show or suggest a base having a plurality of reaction wells formed therein, each of the reaction wells having a permanently closed lower end and an open upper end for receiving components for the reaction, as required by claims 52 and 53.

Accordingly, claims 2-4, 52, and 53 are submitted as patentable over the prior art of record.

Claim 5 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Cody et al. in view of U.S. Patent No. 3,617,033 (Ichikawa et al.). Ichikawa shows an apparatus for continuous gas-liquid contact. The apparatus may be used, for example, in refining crude terephthalic acid by contacting a suspension thereof with molecular oxygen. The apparatus includes a vertical vessel with a tapered bottom, a pipe for supplying a liquid, an opening for feeding a gas, and an opening for withdrawing the liquid. The reaction vessel may operate at a total pressure of 5-100 atmospheres. The Examiner cited Ichikawa et al. for its use of a titanium pressure vessel. As previously discussed, the apparatus of Cody et al. is designed to operate at very low pressures and would require significant modification for operation substantially above atmospheric pressure, not just with regard to the material of the manifold.

With respect to the rejection of claim 26 over Cody et al. and U.S. Patent No. 6,309,608 (Zhou et al.), the Examiner refers to springs 490 as being used to

bias vials upward against a flow restriction device. Zhou et al., however, teach away from using springs to bias vials against a flow restriction device. Springs 490 of the Zhou et al. apparatus are used to force seal plate 400 towards the bottom surface of reaction block 100 and not for biasing vials (see, Figs. 1 and 5A-5F, and col. 13, line 66- col. 14, line 2). Glass vials are not used in the reaction block 100, because vials would make it impossible to open the reaction wells and drain or purge the contents, which is an important feature of the Zhou et al. apparatus.

The additional references cited including U.S. Patent Nos. 5,529,756 (Brennan et al.), 6,171,555 (Cargill et al.), 6,027,694 (Boulton et al.), 6,264,891 (Heynaker et al.), 5,443,791 (Cathcart et al.), 4,180,943 (Smith et al.), and 6,250,707 (Dinter et al.), do not remedy the deficiencies of the primary references.

III. Conclusion:

In view of the foregoing, reconsideration and allowance of claims 1, 3-37, and 42-53 are respectfully requested. If the Examiner feels that a telephone conference would in any way expedite prosecution of the application, please do not hesitate to call the undersigned at (408) 446-8695.

Respectfully submitted,



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